Urinary Incontinence in a Noncatheterizing Woman With Multiple Sclerosis

NYU Case of the Month, January 2017

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A 67-year-old woman with relapsing remitting multiple sclerosis (MS) was referred for persistent urinary incontinence. She complains of hourly urinary frequency, nocturia four times per night, urinary urgency, and urinary urgency incontinence (UUI); she changes pads five to six times a day. She denies stress urinary incontinence (SUI), hesitancy, or incomplete bladder emptying, and has never required clean intermittent catheterization (CIC). Pelvic floor exercises, multiple anticholinergic agents, and a β-3 agonist have been minimally effective. She had considerable dry mouth from the anticholinergic agents.

Physical Examination

The patient ambulates with a slow, unsteady gait, and requires the aid of a rolling walker. She is cognitively intact and demonstrates good manual dexterity. No significant visual field defects are elicited. Pelvic examination reveals marked incontinence dermatitis of the labia and perineum. No pelvic organ prolapse or SUI is found. The patient is able to mount a very weak contraction of her pelvic floor muscles.

Evaluation

The patient's serum creatinine level is 1.0 mg/dL. Urinalysis results are negative for any abnormalities. Renal bladder ultrasound reveals no hydronephrosis or nephrolithiasis. Her postvoid residual urine volume (PVR) is 0 mL. Magnetic resonance imaging of the brain reveals stable lesions consistent with MS (Figure 1).

Management

After establishing treatment goals and reviewing options for persistent UUI in a woman with MS, she elects to pursue intradetrusor onabotulinumtoxinA injection at a low dose of 100 U in an outpatient

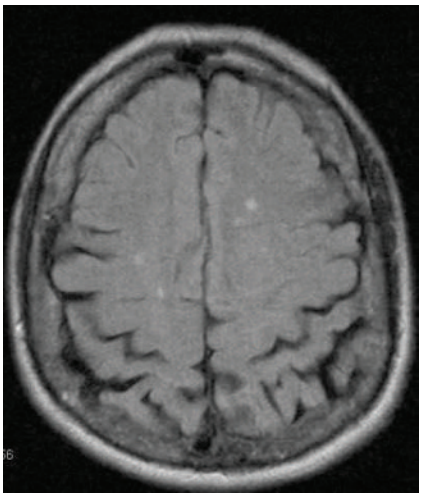

Figure 1. T2-weighted-fluid-attenuated inversion recovery brain magnetic resonance imaging (MRI) scan showing a few demyelinating lesions in the brain. This is consistent with the patient diagnosis of multiple sclerosis and is stable compared with prior MRI scans.

office setting with local anesthetic. She is sent home on a short course of oral antibiotics.

Two weeks following injection, her condition has dramatically improved; she is voiding four to five times daily, with one episode of nocturia per night. She uses one thin panty liner a day. Her PVR is 115 mL. By 9 months, her urgency starts to return gradually, and she undergoes another onabotulinumtoxinA injection.

Comment

Neurogenic lower urinary tract dysfunction is prevalent in the MS population. Anticholinergic therapy has been the mainstay of therapy for neurogenic detrusor overactivity (NDO) for many years. Long-term utilization of anticholinergic therapy in the idiopathic overactive bladder population is shockingly low, with termination of therapy in up to 92% of patients at 2 years.[1] A similar trend is suggested in the MS NDO population. Inadequate efficacy and intolerable side effects contribute to the cessation of therapy.

Our patient was offered a trial of mirabegron, which I commonly use in MS patients with UUI due to theoretically better tolerance and absence of constipation. Our initial experience has shown that β-3 agonists exhibit statistically significant improvement in patients with overactive bladder symptom compared with baseline, with an improvement in constipation.[2] Although promising, this represents only preliminary exploratory open-label data. Larger controlled trials are needed to confirm such findings.

OnabotulinumtoxinA received US Food and Drug Administration approval for the treatment of NDO in 2011. The two large, phase 3 trials included a large number of MS patients; however, this therapy is still not ubiquitous. One limitation in the MS population is failure to access appropriate urologic care.[3] Neurologists at the NYU Langone MS Comprehensive Care Center now utilize a screening tool for NDO to overcome our patients' perspective that neurologists fail to ask about bladder issues.

It is often asked if urodynamic testing is needed before injecting onabotulinumtoxinA. Women with MS are not usually considered at high risk for upper tract deterioration. Our patient emptied her bladder completely, had a normal renal ultrasound result, stable renal function, and unchanged neurologic status, suggesting urodynamics would be low yield.

The approved dose of onabotulinumtoxinA in patients with NDO is 200 U; however, in our patient, we elected to use 100 U, which is the approved dose for idiopathic overactive bladder. We recently completed a multicenter placebo-controlled trial of onabotulinumtoxinA, 100 U vs placebo in MS patients who were noncatheterizing.[4] Administration of 100 U for MS-induced NDO again resulted in significant and clinically meaningful improvements in quality of life measures, as well as improvements and resolution of incontinence episodes (Figure 2). Comparing the results of this trial with the original pooled phase 3 data (specifically in noncatheterizing MS patients treated with 200 U), the requirement for CIC after injection was much lower (only 15.2% with 100 U vs 31.4% with 200 U; this trial was

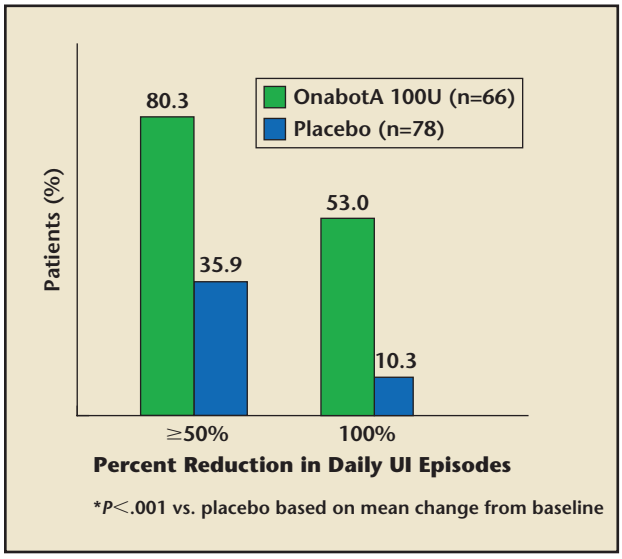

Figure 2. Proportions of noncatheterizing multiple sclerosis patients who achieved ≥ 50% and 100% reductions in daily UI episodes at week 6. OnabotA, onabotulinumtoxinA; UI, urinary incontinence. Adapted from Denys P et al.[4]

not meant to serve as a direct comparison of two doses of onabotulinumtoxinA in noncatheterizing MS patients, but did use similar inclusion criteria, endpoints, and adverse event definitions), maintaining durability of response.[5]

Finally, appropriate follow-up of patients after injection is key to success with onabotulinumtoxinA. Noncatheterizing NDO patients should be seen at 2 weeks to assess urinary symptoms and ensure appropriate bladder emptying. Our patient had a PVR of 115 mL, well below the threshold to consider CIC. In women with symptomatic improvement, PVR up to 350 mL is tolerated before considering temporary CIC. Patients are told in advance to expect repeat injection once or twice a year. Scheduled follow-up prevents patients from being incontinent again before calling to arrange a repeat injection. In response to onabotulinumtoxinA injections, our patient stated she "hasn't felt this good in the past 15 years!" ■

References

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